



## Complete Summary

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### GUIDELINE TITLE

Reduction of the influenza burden in children.

### BIBLIOGRAPHIC SOURCE(S)

Reduction of the influenza burden in children. Pediatrics 2002 Dec; 110(6):1246-52. [58 references]

## COMPLETE SUMMARY CONTENT

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## SCOPE

### DISEASE/CONDITION(S)

Influenza

### GUIDELINE CATEGORY

Prevention  
Treatment

### CLINICAL SPECIALTY

Allergy and Immunology  
Dermatology  
Family Practice  
Infectious Diseases  
Internal Medicine  
Obstetrics and Gynecology  
Otolaryngology  
Pediatrics  
Preventive Medicine  
Pulmonary Medicine

## INTENDED USERS

Advanced Practice Nurses  
Health Care Providers  
Physician Assistants  
Physicians  
Public Health Departments

## GUIDELINE OBJECTIVE(S)

To present recommendations for reducing the influenza burden in children

## TARGET POPULATION

Healthy children between 6 and 24 months of age, children and adolescents at high risk for hospitalization or complications due to influenza, women in their second or third trimester of pregnancy during influenza season, and persons in close contact with high-risk children such as:

- All health care personnel in contact with pediatric patients in hospital and outpatient settings
- Household contacts, including siblings and primary caregivers
- Children who are members of households with high-risk adults, including those with symptomatic HIV infection
- Home caregivers for children and adolescents in high-risk groups

## INTERVENTIONS AND PRACTICES CONSIDERED

1. Influenza vaccines
  - Trivalent inactivated influenza vaccine (TIV) (Fluzone, Fluvirin, FluShield)
  - Trivalent live-attenuated, cold-adapted influenza vaccine (T-CAIV) (not approved by the Food and Drug Administration at time of writing)
2. Antiviral medication
  - Amantadine hydrochloride
  - Rimantadine hydrochloride
  - Zanamivir (Relenza)
  - Oseltamivir phosphate (Tamiflu)

## MAJOR OUTCOMES CONSIDERED

- Vaccine coverage
- Incidence and duration of influenza
- Incidence of influenza complications
- Costs of influenza immunizations
- Number of antibiotic prescriptions
- Adverse effects of influenza vaccine

## METHODOLOGY

## METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

#### DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

#### NUMBER OF SOURCE DOCUMENTS

Not stated

#### METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

#### RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

US Preventive Services Task Force System of Quality of Scientific Evidence

I: Evidence obtained from at least 1 properly designed, randomized controlled trial

II-1: Evidence obtained from well-designed controlled trials without randomization

II-2: Evidence obtained from well-designed cohort or case-control analytic studies, preferentially from more than 1 center or group

II-3: Evidence obtained from multiple time series with or without the intervention, or dramatic results in uncontrolled experiments (such as the results of the introduction of penicillin treatment in the 1940s)

III: Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees

#### METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

#### DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

#### METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

#### RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

## COST ANALYSIS

Whether universal immunization of young children would result in a net cost or a net savings to society depends on the influenza attack rate, the rates of health outcomes (ie, outpatient visits, hospitalizations, and deaths), and the cost of immunization. The attack rate and rates of health outcomes can vary considerably from year to year, and regional variation in both of these factors is possible within a given season. These variations make it impossible to generate a single precise estimate of the cost-effectiveness or the cost-benefit of universal immunization of children.

The total cost of immunizing a single child includes direct and indirect costs. The direct costs include supplies (eg, syringe, vaccine), personnel, and administrative expenses. Indirect costs can be a significant component of the total cost of immunization. One of the most important factors is the time lost from work by caregivers of children to be immunized. Three studies have suggested that universal childhood immunization may be cost-saving if immunizations could be performed in a group-based setting, such as an after-hours or weekend immunization clinic that would not require a parent to miss work. A subcommittee of the Advisory Committee on Immunization Practices, after a review of the major economic studies of influenza immunization, concluded that it is unlikely that universal influenza immunization of young children will generate savings, from a societal perspective, unless the total costs of immunization are less than \$20 to \$25 per child immunized (M. Meltzer, oral presentation at Advisory Committee on Immunization Practices Influenza Workshop, Atlanta, GA, September 11, 2001).

## METHOD OF GUIDELINE VALIDATION

Peer Review

## DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

## RECOMMENDATIONS

### MAJOR RECOMMENDATIONS

Note from the National Guideline Clearinghouse (NGC) and the American Academy of Pediatrics (AAP): On December 11, 2003, AAP released additional information for clinicians regarding the prioritization of remaining influenza vaccine supplies during the 2003 shortage. This information is available from the [AAP Web site](#).

Note: Definitions for the strength of the evidence (I-III) are given at the end of the Major Recommendations.

1. Practitioners should increase their efforts through tracking and recall systems to ensure that children traditionally considered at high risk of severe disease and complications from influenza receive annual immunization. High-risk

children and adolescents who should receive priority for influenza immunization are those with the following (evidence grade II-3):

- Asthma or other chronic pulmonary diseases, such as cystic fibrosis
- Hemodynamically significant cardiac disease
- Immunosuppressive disorders or therapy
- Human immunodeficiency virus (HIV) infection
- Sickle cell anemia and other hemoglobinopathies
- Diseases requiring long-term aspirin therapy, such as rheumatoid arthritis or Kawasaki syndrome
- Chronic renal dysfunction
- Chronic metabolic disease, such as diabetes mellitus

Other individuals who should receive priority for influenza immunization include:

- Women who will be in their second or third trimester of pregnancy during the influenza season (evidence grade II-3)
  - Persons who are in close contact with high-risk children, including (evidence grade II-3):
    - All health care personnel in contact with pediatric patients in hospital and outpatient settings
    - Household contacts, including siblings and primary caregivers, of high-risk children
    - Children who are members of households with high-risk adults, including those with symptomatic HIV infection
    - Home caregivers for children and adolescents in high-risk groups
2. Young, healthy children also are at high risk of hospitalization for influenza infection; therefore, the American Academy of Pediatrics encourages influenza immunization of healthy children between 6 and 24 months of age to the extent logistically and economically feasible (evidence grade II-3). This applies to any child who will be 6 through 23 months of age anytime during influenza season, which extends from the beginning of October through March. Children should not be immunized before they reach 6 months of age. Influenza immunization of household contacts and out-of-home caregivers of children younger than 24 months also is encouraged when feasible (evidence grade III). Immunization of close contacts of children younger than 6 months may be particularly important, because these infants will not be immunized.
3. Antiviral drugs are an adjunct to, not a substitute for, the prevention of influenza with immunization. Amantadine and rimantadine are licensed for chemoprophylaxis of influenza A in children 1 year or older. Oseltamivir may be used for prevention of influenza A and B in persons 13 years and older (evidence grade I). Chemoprophylaxis may be considered for the following situations (evidence grade III):
- Protection of high-risk children during the 2 weeks after immunization while an immune response is developing or if the children are immunized after influenza circulation has been documented
  - Protection of high-risk children for whom the vaccine is contraindicated (i.e., those with a history of anaphylactic reaction to eggs)
  - Protection of nonimmunized close contacts of high-risk children
  - Protection of immunocompromised children who may not respond to vaccine

- Control of influenza outbreaks in a closed setting, such as an institution with high-risk children
- Protection of immunized high-risk individuals if vaccine strain poorly matches circulating influenza strain(s)

#### US Preventive Services Task Force Rating System of Quality of Scientific Evidence

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II-1: Evidence obtained from well-designed controlled trials without randomization

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III: Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees

#### CLINICAL ALGORITHM(S)

None provided

### EVIDENCE SUPPORTING THE RECOMMENDATIONS

#### TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (See the "Major Recommendations" field).

### BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

#### POTENTIAL BENEFITS

- Appropriate and timely use of antiviral agents against influenza A and B
- Decreased nosocomial transmission
- Decreased unnecessary antimicrobial use
- Decreased complications of influenza

Subgroups Most Likely to Benefit:

Children considered at high risk of severe disease and complications from influenza infection are those with:

- Asthma or other chronic pulmonary diseases, such as cystic fibrosis

- Hemodynamically significant cardiac disease
- Immunosuppressive disorders or therapy
- HIV infection
- Sickle cell anemia and other hemoglobinopathies
- Diseases requiring long-term aspirin therapy, such as rheumatoid arthritis or Kawasaki disease
- Chronic renal dysfunction
- Chronic metabolic disease, such as diabetes mellitus

## POTENTIAL HARMS

### Trivalent Inactivated Influenza Vaccine (TIV)

- The most common adverse effects associated with TIV are soreness at the injection site and fever. More subjective symptoms, such as nausea, lethargy, headache, muscle aches, and chills, are also reported.
- An increase in the number of cases of Guillain-Barré Syndrome (GBS) was reported after the "swine flu" vaccine program in 1976. Intensive surveillance for GBS cases demonstrated a relative risk of 6.2 in immunized versus nonimmunized adults during the 10 weeks after administration of vaccine. This translates into fewer than 10 cases per million immunized. Additional investigation revealed that in 3 of 4 influenza seasons studied (between 1977 and 1981), the overall relative risk estimates for GBS after influenza immunization were slightly increased, but the difference was not significant. The most recent study of GBS and influenza vaccine examined the 1992-1993 and 1993-1994 seasons and showed a relative risk of GBS of 1.7, which just met significance (95% confidence intervals [CI]: 1.0-2.8;  $P = .04$ ). The number of cases was shown to peak 2 weeks after immunization. Thus, it appears that there may be a slight increase in the risk of GBS (approximately 1 additional case of GBS per 1 million vaccine recipients) among adults after influenza immunization, at least in some years. Rare cases of GBS after TIV immunization in children have been reported.
- Studies of the safety of TIV immunization of children and adults with human immunodeficiency virus (HIV) infection have yielded conflicting results. Some have demonstrated a transient (2- to 8-week) increase in HIV-1 replication and/or a decrease in CD4+ T-lymphocyte cell counts, but others have shown no significant effect. Most experts believe that the benefits of immunization of children with HIV infection outweigh possible risks.
- Allergic Reactions to TIV -- Urticarial reactions to TIV have been reported.

### Antiviral Medication

- Amantadine and rimantadine may cause reversible adverse effects on the central nervous system, including nervousness, lightheadedness, difficulty with concentration, and rarely, tremors or seizures.
- Gastrointestinal disturbances occurred in 14.3% of oseltamivir recipients.
- Oseltamivir is associated with nausea and vomiting in approximately 10% of recipients. These adverse effects may be decreased if the drug is taken with food, which does not affect peak plasma concentration or bioavailability.

### Subgroups Most Likely to be Harmed:

## Inactivated Influenza Vaccine

- Fever is more common in children younger than 2 years (10%-35% of recipients), usually occurring 6 to 24 hours after immunization. Local reactions occur in approximately 6% of young children given the split-virus vaccine.
- It is unknown whether influenza immunization of individuals with a history of GBS increases the recurrence rate.
- Because influenza vaccine is grown in embryonated eggs, children demonstrating severe anaphylactic reaction to chicken or egg proteins rarely can experience a similar type of reaction to influenza vaccine and generally should not receive inactivated influenza vaccine.
- Inactivated influenza containing thimerosal should not be given to individuals with hypersensitivity to thimerosal.

## Antiviral Medication

- Amantadine and rimantadine are excreted in the urine, and dosage adjustments are necessary for children with renal disease.
- Rimantadine undergoes metabolism in the liver before renal excretion, so adjustment of dosage is suggested for patients with severe liver disease.
- Some patients with a history of asthma have experienced bronchospasm; therefore, zanamivir is generally not recommended for patients with underlying airway disease.

## QUALIFYING STATEMENTS

### QUALIFYING STATEMENTS

The recommendations in this statement do not indicate an exclusive course of treatment or serve as a standard of medical care. Variations, taking into account individual circumstances, may be appropriate.

## IMPLEMENTATION OF THE GUIDELINE

### DESCRIPTION OF IMPLEMENTATION STRATEGY

In October 2003, the American Academy of Pediatrics (AAP) released additional guidance for clinicians concerning implementation of the December 2002 policy, "encouraging, when feasible, influenza vaccine to children 6-24 months of age" because of the increased risk of hospitalization and serious infection in young children, especially infants. This document is available from the [AAP Web site](#).

## INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

### IOM CARE NEED

Staying Healthy



## IOM DOMAIN

Effectiveness  
Patient-centeredness  
Timeliness

## IDENTIFYING INFORMATION AND AVAILABILITY

### BIBLIOGRAPHIC SOURCE(S)

Reduction of the influenza burden in children. Pediatrics 2002 Dec; 110(6): 1246-52. [58 references]

### ADAPTATION

Not applicable: The guideline was not adapted from another source.

### DATE RELEASED

2002 Dec

### GUIDELINE DEVELOPER(S)

American Academy of Pediatrics - Medical Specialty Society

### SOURCE(S) OF FUNDING

American Academy of Pediatrics

### GUIDELINE COMMITTEE

Committee on Infectious Diseases

### COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

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Consultant: Edgar O. Ledbetter, MD

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#### FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

#### GUIDELINE STATUS

This is the current release of the guideline.

American Academy of Pediatrics (AAP) Policies are reviewed every 3 years by the authoring body, at which time a recommendation is made that the policy be retired, revised, or reaffirmed without change. Until the Board of Directors approves a revision or reaffirmation, or retires a statement, the current policy remains in effect.

#### GUIDELINE AVAILABILITY

Electronic copies: Available from the [American Academy of Pediatrics \(AAP\) Policy Web site](#).

Print copies: Available from AAP, 141 Northwest Point Blvd., P.O. Box 927, Elk Grove Village, IL 60009-0927.

#### AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Rennels MB, Meissner HC. Technical report: reduction of the influenza burden in children. Pediatrics 2002 Dec; 110(6): e80. Electronic copies: Available from the [American Academy of Pediatrics \(AAP\) Policy Web site](#)
- Influenza vaccine implementation information for 2003-2004. Elk Grove Village (IL): American Academy of Pediatrics; 2003 Oct 10. 6 p. Electronic copies: Available from the [AAP Web site](#).
- Prevention of influenza in children during vaccine shortage. Elk Grove Village (IL): American Academy of Pediatrics; 2003 Dec 11. 2 p. Electronic copies: Available from the [AAP Web site](#).

Print copies: Available from the American Academy of Pediatrics, 141 Northwest Point Blvd., P.O. Box 927, Elk Grove Village, IL 60009-0927.

#### PATIENT RESOURCES

None available

#### NGC STATUS

This NGC summary was completed by ECRI on May 15, 2003. The information was verified by the guideline developer on June 9, 2003.

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